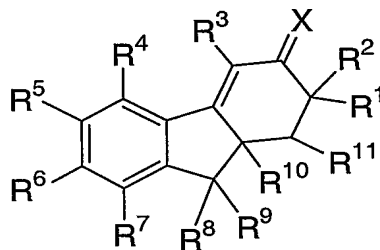


WHAT IS CLAIMED IS:

1. The use of an ER β agonist for the preparation of a medicament useful in the treatment of hypertension, cardiac dysfunction or stroke, in a mammal in need thereof.

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2. The use according to Claim 1 wherein the agonist is a compound of the formula:



wherein X is O or N-OR^a;

R¹ is hydrogen or C₁₋₆alkyl;

10 R² is hydrogen, hydroxy, iodo, or C₁₋₆alkyl;

R³ is hydrogen, chloro, bromo, iodo, cyano, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, aryl or heteroaryl, wherein said alkyl, alkenyl, aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 groups selected from the group consisting of fluoro, chloro, bromo, iodo, cyano, OR^a, NR^aR^c, C(=O)R^a, CO₂R^c, NR^aC(=O)R^c, CONR^aR^c, CSNR^aR^c, SR^a, YR^d and ZYR^d;

15 R⁴ is hydrogen, fluoro, hydroxy or methyl;

R⁵ is hydrogen, fluoro, chloro or bromo;

R⁶ is OR^a, O(C=O)R^c, amino or NH(C=O)R^c;

R⁷ is hydrogen, NR^bR^c, fluoro, chloro, bromo, nitro or C₁₋₆alkyl;

R⁸ is hydrogen or C₁₋₆alkyl;

20 R⁹ is hydrogen or C₁₋₆alkyl;

or R⁸ and R⁹, when taken together with the carbon atom to which they are attached, form a carbonyl group;

R¹⁰ is hydrogen, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₃₋₆cycloalkyl or cycloalkylalkyl, wherein said alkyl, alkenyl, cycloalkyl and cycloalkylalkyl groups are optionally substituted with OR^b, SR^b, C(=O)R^b, or 1-5 fluoro;

25

or R¹⁰ and R¹¹, when taken together with the three intervening carbon atoms to which they are attached, form a 5-6 membered cycloalkyl ring which is optionally substituted with C₁₋₆alkyl;

R¹¹ is hydrogen or C₁₋₄alkyl;

R^a is hydrogen, C₁₋₁₀alkyl, or phenyl, wherein said alkyl group can be optionally substituted with

30 hydroxy, amino, O(C₁₋₄alkyl), NH(C₁₋₄alkyl), N(C₁₋₄alkyl)₂, phenyl, or 1-5 fluoro;

R^b is hydrogen, C₁₋₁₀alkyl, benzyl or phenyl;

R^c is hydrogen, C₁₋₁₀alkyl or phenyl;

or R^a and R^c, whether or not on the same atom, can be taken together with any attached and intervening atoms to form a 4-7 membered ring;

5 R^d is NR^bR^c, OR^a, CO₂R^a, O(C=O)R^a, CN, NR^c(C=O)R^b, CONR^aR^c, SO₂NR^aR^c, or a 4-7 membered N-heterocycloalkyl ring that is optionally interrupted by O, S, NR^c, or C=O;

Y is CR^bR^c, C₂₋₆ alkylene or C₂₋₆ alkenylene, wherein said alkylene and alkenylene linkers are optionally interrupted by O, S, or NR^c;

Z is O, S, NR^c, C=O, O(C=O), (C=O)O, NR^c(C=O) or (C=O)NR^c;

10 or a salt or stereoisomer thereof.

3. The use according to Claim 2 wherein X is O, N-OH or N-OCH₃.

4. The use according to Claim 3 wherein R⁶ is OR^a or O(C=O)R^c.

15

5. The use according to Claim 4 wherein R³ is hydrogen, chloro, bromo, iodo, cyano, C₁₋₁₀alkyl, aryl or heteroaryl, wherein said alkyl, aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 groups selected from the group consisting of fluoro, chloro, bromo, cyano, NR^aR^c, C(=O)R^a, CO₂R^c, CONR^aR^c, SR^a, YR^d, and ZYR^d.

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6. The use according to Claim 2 wherein the agonist is:

4-bromo-7-hydroxy-9a-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

9a-butyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

(3E)-9a-butyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one oxime;

25 9a-[(1E)-1-butenyl]-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

4-bromo-9a-butyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

4-bromo-9a-butyl-3-methylene-2,3,9,9a-tetrahydro-1H-fluoren-7-ol;

9a-butyl-4-cyano-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

4-benzyl-9a-butyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

30 9a-butyl-7-hydroxy-4-(2-thienyl)-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

9a-butyl-7-hydroxy-4-{4-[2-(1-piperidinyl)ethoxy]phenyl}-1,2,9,9a-tetrahydro-3H-fluoren-3-one hydrochloride;

9a-butyl-7-hydroxy-4-(4-hydroxyphenyl)-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

(2E)-3-[4-(9a-butyl-7-hydroxy-3-oxo-2,3,9,9a-tetrahydro-1H-fluoren-4-yl)phenyl]-2-propenoic acid;

35 9a-butyl-7-hydroxy-8-methyl-1,2,9,9a-3H-tetrahydro-fluoren-3-one;

- 4-bromo-9a-butyl-7-hydroxy-8-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a butyl-4,8-dimethyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-8-chloro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-9a-butyl-2,4-dimethyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
5 (2SR,9aRS)-9a-butyl-2,4-dimethyl-7-hydroxy-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-7-hydroxy-2,2,4-trimethyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aRS)-9a-butyl-7-hydroxy-2-iodo-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aRS)-9a-butyl-2,7-dihydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2RS,9aSR)-9a-butyl-7-hydroxy-2-(2-hydroxyethyl)-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
10 (2SR,9aSR)-2-allyl-9a-butyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2RS,9aSR)-9a-butyl-7-hydroxy-2-(3-hydroxy-2-oxopropyl)-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(9SR,9aSR)-7-hydroxy-4-methyl-9-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-8-chloro-7-hydroxy-4-(trifluoromethyl)-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
15 4-acetyl-9a-butyl-8-chloro-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-8-chloro-4-cyano-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-4-ethyl-6-fluoro-7-hydroxy-8-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-8-chloro-6-fluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-8-chloro-4-ethyl-6-fluoro-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
20 4-bromo-9a-butyl-8-chloro-6-fluoro-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-8-chloro-6-fluoro-7-hydroxy-4-(trifluoromethyl)-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
2-hydroxy-5-methylgibba-1(10a),2,4,4b-tetraen-6-one;
4-bromo-9a-butyl-3-oxo-2,3,9,9a-1H-fluoren-7-yl pivalate;
7-hydroxy-4,9a-dimethyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
25 9a-ethyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
7-hydroxy-4-methyl-9a-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
7-hydroxy-9a-isobutyl-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-4-ethyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-7-hydroxy-4-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
30 4,9a-dibutyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-4-chloro-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-7-hydroxy-4-iodo-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-7-hydroxy-4-trifluoromethyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-7-hydroxy-4-phenyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
35 9a-butyl-4-(2-furyl)-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

- 7-hydroxy-9a-(3-iodopropyl)-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
7-hydroxy-4-methyl-9a-(2-methyl-1-propenyl)-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-4-{4-[2-(dimethylamino)ethoxy]phenyl}-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one
hydrochloride;
5 9a-butyl-4-{4-[2-(diethylamino)ethoxy]phenyl}-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one
hydrochloride;
9a-butyl-7-hydroxy-4-{4-[2-(1-pyrrolidinyl)ethoxy]phenyl}-1,2,9,9a-tetrahydro-3H-fluoren-3-one
hydrochloride;
9a-butyl-7-hydroxy-4-{4-[2-(4-morpholinyl)ethoxy]phenyl}-1,2,9,9a-tetrahydro-3H-fluoren-3-one
10 hydrochloride;
9a-butyl-4-{4-[3-(dimethylamino)propoxy]-phenyl}-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one
hydrochloride;
9a-butyl-7-hydroxy-4-{4-[3-(1-piperidinyl)propoxy]phenyl}-1,2,9,9a-tetrahydro-3H-fluoren-3-one
hydrochloride;
15 (3E)-9a-butyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one O-methyloxime;
(2SR,9aSR)-9a-butyl-2-ethyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-9a-butyl-7-hydroxy-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-9a-butyl-7-hydroxy-4-methyl-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-4,9a-dibutyl-7-hydroxy-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
20 (2SR,9aSR)-4-bromo-9a-butyl-7-hydroxy-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2RS,9aSR)-9a-butyl-7-hydroxy-2-(2-oxoethyl)-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-2,9a-dibutyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2RS,9aRS)-9a-butyl-7-hydroxy-2,4-dimethyl-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-butyl-7-hydroxy-2,2-dipropyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
25 9a-butyl-7-hydroxy-4-methyl-2,2-dipropyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aRS)-9a-butyl-2,7-dihydroxy-4-methyl-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
4-bromo-9a-butyl-2,2-diethyl-7-hydroxy-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-7-hydroxy-2,4,9a-trimethyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
(2SR,9aSR)-7-hydroxy-4,9a-dimethyl-2-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
30 (2SR,9aSR)-9a-butyl-8-chloro-2-ethyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
8-chloro-9a-ethyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
8-bromo-9a-ethyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
9a-ethyl-7-hydroxy-4,8-dimethyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
8-chloro-7-hydroxy-4-methyl-9a-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
35 8-bromo-7-hydroxy-4-methyl-9a-propyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;

- 7-hydroxy-4,8-dimethyl-9a-propyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-chloro-7-hydroxy-4-methyl-9a-[(1*E*)-1-propenyl]-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-bromo-9a-butyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-butyl-7-hydroxy-4,8-dimethyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
5 9a-butyl-7-hydroxy-4-methyl-8-nitro-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-amino-9a-butyl-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-butyl-7-hydroxy-4-(4-hydroxyphenyl)-8-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-butyl-7-hydroxy-8-methyl-4-{4-[2-piperidiny]-ethoxy}phenyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
4-bromo-7-hydroxy-9a-propyl-1*H*-fluorene-3,9(2*H*,9*aH*)-dione;
10 4,8-dibromo-7-hydroxy-9a-propyl-1*H*-fluorene-3,9(2*H*,9*aH*)-dione;
4-bromo-9a-butyl-7-hydroxy-6-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-butyl-8-chloro-4-methyl-3-oxo-2,3,9,9a-tetrahydro-1*H*-fluoren-7-yl pivalate;
9a-butyl-6,8-difluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-butyl-4-ethyl-6,8-difluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
15 4-bromo-9a-butyl-6,8-difluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-bromo-9a-butyl-4-chloro-8-difluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-butyl-4,8-dibromo-6-fluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-ethyl-6-fluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-ethyl-6,8-difluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
20 8-chloro-9a-ethyl-6-fluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-bromo-9a-ethyl-6-fluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-ethyl-6-fluoro-7-hydroxy-4,8-dimethyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
4,9a-diethyl-6,8-difluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
4-bromo-8-chloro-9a-ethyl-6-fluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
25 4-bromo-8-chloro-9a-(cyclopentylmethyl)-6-fluoro-7-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-ethyl-5-fluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-bromo-9a-ethyl-5-fluoro-7-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-ethyl-6,7-dihydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
8-bromo-9a-ethyl-6,7-dihydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
30 9a-ethyl-6-hydroxy-4-methyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
9a-ethyl-6-hydroxy-4-vinyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
4-allyl-9a-ethyl-6-hydroxy-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;
2-hydroxy-5-methyl-7,8,9,10-tetrahydro-7,10a-methanocycloocta[*a*]inden-6(11*H*)-one;
7-amino-4-bromo-9a-butyl-1,2,9,9a-tetrahydro-3*H*-fluoren-3-one;

7-amino-4,8-dibromo-9a-ethyl-1,2,9,9a-tetrahydro-3H-fluoren-3-one;
or a salt or stereoisomer thereof.

5 7. The use according to Claim 1 which further comprises an antihypertensive agent selected from the group consisting of a calcium channel blocking agent, a beta-adrenergic blocking agent, an angiotensin-converting enzyme inhibitor, angiotensin-II receptor antagonist, a thiazide diuretic and a peripheral vasodilator.

10 8. The use according to Claim 7 wherein the calcium channel blocking agent is bepridil, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nimodipine, verapamil or amlodipine.

15 9. The use according to Claim 8 wherein the beta-adrenergic blocking agent is acebutolol, atenolol, betaxolol, bisoprolol, carteolol, labetalol, metoprolol, nadolol, penbutolol, pindolol, propranolol, sotalol or timolol.

 10. The use according to Claim 7 wherein the angiotensin-converting enzyme inhibitor is benazepril, captopril, cilazapril, enalapril, enalaprilat, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril ortrandolapril.

20 11. The use according to Claim 7 wherein the angiotensin-II receptor antagonist is losartan, valsartan, irbesartan, candesartan, telmisartan or eprosartan.

 12. The use according to Claim 11 wherein the angiotensin-II receptor antagonist is losartan.

25 13. The use according to Claim 7 wherein the thiazide diuretic is bendroflumethiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazde, methyclothiazide, metolazone, polythiazide, quinethazone or trichlormethiazide.

30 14. The use according to Claim 7 wherein the peripheral vasodilator is hydralazine, isoxuprine or minoxidil.

 15. A pharmaceutical composition comprising an ER β agonist, an antihypertensive agent and a pharmaceutically acceptable carrier.

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